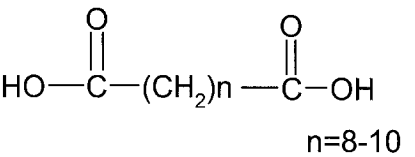
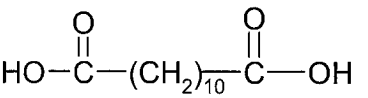
November 19, 2003

ROBUST SUMMARY FOR CORFREE® M1

Summary

Corfree® M1 is a mixture of dibasic acids, primarily dodecanedioic acid (DDDA) (~38-49%) and undecanedioic acid (~31-38%). The mixture also includes sebacic acid (~5-7%), other dibasic acids (~9-19%), other organics (~7-11%), nitrogen (~0.5%), and water (~0.3%). Available data are presented in this document on Corfree® M1 as well as DDDA (the largest component of the mixture). DDDA is not in the HPV program as it has previously been submitted under the Organisation for Economic Co-operation and Development (OECD) Screening Information Data Set (SIDS) Program (IPCS, n.d.); however, data will be presented on DDDA as it is the largest component in the Corfree® M1 mixture. A search of available toxicology data for undecanedioic acid (the second largest component of the mixture) did not produce any information.

Chemical Name	CAS Registry Number	Structure
Reaction product (cyclododecanol/ cyclododecanone/nitric acid) high-boiling fraction [referred to in document as Corfree® M1]	72162-23-3	 n=8-10
Dodecanedioic acid	693-23-2	

Scientific literature was searched and summarized (Table 1). Each study on these materials was evaluated for adequacy. Robust summaries were developed for each study addressing specific SIDS endpoints. Summaries were also developed for studies either considered not adequate but provided information of relevance for hazard identification and evaluation, or covered non-SIDS endpoints (Appendices A and B).

Table 1: Matrix of Available and Adequate Data on Corfree® M1 and DDDA

	Corfree® M1	DDDA
PHYSICAL/CHEMICAL CHARACTERISTICS		
Melting Point	√	√
Boiling Point	N/A	√
Vapor Pressure	√	√
Partition Coefficient	–/*	√
Water Solubility	–/*	√
ENVIRONMENTAL FATE		
Photodegradation	√	√
Stability in Water	√	√
Transport (Fugacity)	–/*	√
Biodegradation	√	√
ECOTOXICITY		
Acute Toxicity to Fish	–/*	√
Acute Toxicity to Invertebrates	√	√
Acute Toxicity to Aquatic Plants	–/*	√
MAMMALIAN TOXICITY		
Acute Toxicity	√	√
Repeated Dose Toxicity	–/*	√
Developmental Toxicity	–/*	√
Reproductive Toxicity	–/*	√
Genetic Toxicity Gene Mutations	√	√
Genetic Toxicity Chromosomal Aberrations	–/*	√/*

√ = Data are available and considered adequate.
√/* = No clastogenicity studies were available; however, an *in vivo* micronucleus study is available and will cover this endpoint.
–/* = No studies were available; however, results similar to DDDA are expected.
N/A = Not Applicable

Evaluation of Data Matrix Patterns

The available adequate data were broken out by discipline (physical/chemical, environmental fate, ecotoxicology, and mammalian toxicology). These comparisons were conducted to determine if a pattern existed among the materials and to determine if additional testing needed to be conducted to complete the data set for Corfree® M1.

Corfree® M1 and DDDA have roughly equivalent physical/chemical properties as a result of structural similarity. Complete and adequate data (Table 2) correlate well with structure and

validate the proposal to use the DDDA dataset to evaluate the toxicity of Corfree® M1. Corfree® M1 is a flaked solid with an average molecular weight of 215. Corfree® M1 softens at 85-95°C, has a flash point of 190°C, specific gravity of 1.02, and negligible vapor pressure at 25ºC. DDDA is also a flaked solid and has a molecular weight of 230. DDDA melts at ca. 128°C, has a flash point of 220°C, specific gravity of 1.15, and vapor pressure of 21 mm Hg at 222°C.

Table 2: Physical and Chemical Characteristics

	Corfree® M1	**DDDA**
Physical Appearance	Solid white odorless flakes	Solid white odorless flakes
Molecular Weight	215	230.31
Water Solubility	No Data	30 mg/L @ 23°C
Melting Point	85-95°C (softens)	ca. 128°C
Boiling Point	Not applicable	250°C @ 48 mm Hg
Vapor Pressure	Negligible @ 25°C	21 mm Hg @ 222ºC
Density/ Specific Gravity	1.02	1.15
Partition Coefficient (Log Kow)	No Data	3.18

DDDA is readily biodegradable. Additional environmental fate data for DDDA are generally not available. A review of estimated physical/chemical properties and environmental-fate characteristics based on output from EPIWIN 3.05 modeling software (Syracuse Research Corporation) indicates that it is unlikely to represent a hazard as a persistent and/or bioaccumulative chemical. When modeled using a Level III fugacity model under a standard scenario of equal emissions to air, water, and soil, DDDA is expected to partition primarily into soil and water compartments. At environmental pH, DDDA will be mostly in an ionized form when dissolved in water. Hydrolytic decomposition is not expected to readily transform DDDA, but it may be subject to photodegradation.

Data on environmental fate are generally not available for Corfree® M1. As a mixture, Corfree® M1 cannot be modeled for environmental fate characteristics. The reported components of the mixture were modeled individually. A review of estimated physical/chemical properties and environmental-fate characteristics based on output from EPIWIN 3.05 modeling software (Syracuse Research Corporation) indicates that the reported products in the Corfree® M1 mixture are unlikely to represent a hazard as persistent and/or bioaccumulative chemicals. The components are expected to generally behave in a manner similar to the C12 component, DDDA. Experimental data on biodegradation of Corfree® M1 show that it is

biodegradable, but did not qualify as readily biodegradable. Biodegradation test results for a mixture are difficult to interpret. The overall slower rate of degradation may indicate that one or more components had a degradation rate slower than that of DDDA. Alternatively, the well known diauxic growth phenomenon (Brock et al., 1984) causes sequential degradation starting with the most preferred substrate. Sequential utilization in a mixture can result in the total biodegradation of carbon in the mixture occurring at a slower rate that the rate for any one component.

Since the individual components of Corfree® M1 do not pose an environmental fate risk, Corfree® M1 should not pose an environmental fate risk and no environmental fate testing is recommended for Corfree® M1.

Table 3: Environmental Fate

	Corfree® M1	**DDDA**
Bioaccumulation*	No Data	BCF = 3.16
Biodegradation	Not readily biodegradable	Readily biodegradable
Fugacity*	No Data	Air 0% Water 18.5% Soil 81.1% Sediments 0.31%
* = Modeled data		

Modeling of physical/chemical parameters (i.e., Kow) and aquatic toxicity was conducted to help provide insight into the behavior in the environment and the aquatic toxicity of DDDA. Syracuse Research Corporation models for estimating physical/chemical properties were used to estimate $\log_{10}$ Kow (Meylan and Howard, 1995) for subsequent use in the ECOSAR program (Table 1). ECOSAR (Meylan and Howard, 1999) was used to estimate aquatic toxicity data for DDDA to green algae, daphnids (planktonic freshwater crustaceans), and fish. ECOSAR predictions are based on actual toxicity test data for classes of compounds with similar modes of action.

The existing test data, coupled with ECOSAR predictions, indicate that Corfree® M1 is unlikely to be acutely toxic to algae, invertebrates, or fish at environmentally relevant concentrations. The existence of both Corfree® M1 and DDDA as solids at temperatures less than approximately 80ºC supports the low concern for acute aquatic toxicity. The other dibasic acids contained in Corfree® M1 are predicted by ECOSAR to be even less toxic than DDDA.

Table 4: Ecotoxicology

	Corfree® M1	**DDDA**
Log Kow	No Data	3.17 (estimated via KowWin)
Toxicity to Fish (LC_{50} value)	No Data	48-hour > 1000 mg/L*(N)** 96-hour = 136 mg/L (E)**
Toxicity to Invertebrates **(**EC_{50} value)	48-hour > 120 mg/L (N)	24-hour > 27.6 mg/L (N) 48-hour = 158 mg/L (E)**
Toxicity to Algae (EC_{50} value)	No Data	72-hour > 5.8 mg/L (N) 96-hour = 105 mg/L (E)**
E = estimated value, N = value based on nominal test concentrations * Sodium salt of DDDA was tested. ** Greater than the water solubility.		

Acute toxicity data indicate that the chemicals exhibit similar acute toxicity (Table 5). Both chemicals have similar acute oral toxicity with LD_{50}s of > 5000 mg/kg and > 3000 mg/kg for Corfree® M1 and DDDA, respectively. These values represent the highest levels tested in their respective acute oral studies. Dermal LD_{50}s for both chemicals were above the highest levels tested, 2000 mg/kg and 6000 mg/kg respectively for Corfree® M1 and DDDA. Corfree® M1 appears to be more irritating to the skin and eye than DDDA. In addition, DDDA is not a dermal sensitizer.

Table 5: Acute Mammalian Toxicity

	Corfree® M1	**DDDA**
Oral LD_{50}	> 5000 mg/kg	> 3000 mg/kg
Inhalation ALC (4-hour)	No Data	> 4.3 mg/L
Dermal LD_{50} (24-hour)	> 2000 mg/kg	> 6000 mg/kg
Dermal Irritation	Moderate irritant	Not an irritant
Eye Irritation	Moderate irritant	Mild irritant
Dermal Sensitization	No Data	Not a sensitizer

A summary of the available data on repeated dose, developmental, and reproductive toxicity is shown in Table 6. No data were available on Corfree® M1 for repeated dose toxicity, developmental toxicity, or reproductive toxicity. DDDA was tested in a combined repeat dose/reproductive developmental screening test in rats. Dose levels of 100, 500, and 1000 mg/kg were tested. No mortality was observed at any dose level. DDDA did not significantly affect overall body weight, body weight gains, food consumption, or food efficiency in male or female rats which received DDDA via gavage for approximately 50 days. Male rats in the 500 and 1000 mg/kg groups had decreased lymphocyte counts. These were not considered adverse effects of the test substance since no morphological alterations were observed in the spleen, there were no decreases in thymus weights, and normal serum globulin concentrations were present. There were no gross or microscopic changes noted that were attributable to the test substance. Some transient cases of hypoactivity were observed shortly after dosing in the 500 and 1000 mg/kg males and the 1000 mg/kg females. There were no significant differences with respect to reproductive performance in male or female rats. The no-observed-adverse effect level (NOAEL) for the repeat dose, developmental, and reproductive toxicity sections of the study was 1000 mg/kg.

Table 6: Repeated Dose, Developmental, and Reproductive Toxicity

	Corfree® M1	**DDDA**
Repeated Dose Toxicity (NOAEL)	No Data	1000 mg/kg
Developmental Toxicity (NOAEL)	No Data	1000 mg/kg Not a developmental toxin
Reproductive Toxicity (NOAEL)	No Data	1000 mg/kg Not a reproductive toxin

Genetic toxicity data are similar between the chemicals (Table 7). Neither Corfree® M1 nor DDDA were mutagenic in the bacterial reverse mutation assay using *Salmonella typhimurium*. No data were available on the clastogenicity of Corfree® M1; however, DDDA did not induce micronuclei in an *in vivo* mouse micronucleus test.

Table 7: Genetic Toxicity

	Corfree® M1	DDDA
Mutagenicity	Negative	Negative
Clastogenicity	No Data	Negative (micronucleus study)

Overall, the toxicologic database for Corfree® M1 is somewhat limited, but the information available suggests a level of toxicity comparable to DDDA. The 2 chemicals are similar in chemical structure, physical/chemical characteristics, environmental fate, aquatic toxicity, and acute toxicity. Because of these similarities, it is reasonable to conclude that these materials

would behave similarly in the areas where data gaps are evident: ecotoxicity, repeated dose toxicity, developmental toxicity, reproductive toxicity, and clastogenicity.

Exposure Assessment for Corfree® M1

Corfree® M1 is produced at one DuPont facility. Corfree® M1 is a reaction product of the nitric acid oxidation of cyclododecanol/cyclododecanone and is a mixture of dibasic acids, primarily dodecanedioic acid and undecanedioic acid. Corfree® M1 is used as a chemical intermediate in the production of corrosion inhibitors for metalworking fluids, engine coolants, and industrial cleaners.

The potential for exposure is the greatest in the Flaking Bay Area. The site can have approximately 1100 personnel working (construction, contractor, and plant employees). The areas where the substance is manufactured will have 16 total operators during normal operations and 40 people during a shutdown or major construction activity.

The site has effective safety, health, and environmental practices and procedures in addition to engineering controls, environmental controls, and personal protective equipment to control exposure. Adequate safety equipment, such as safety showers, eyewash fountains, and washing facilities, are available in the event of an occupational exposure.

Individuals handling Corfree® M1 should not breathe vapor, mist, or dust and should avoid contact with eyes, skin, and clothing. DuPont practices Responsible Care and assesses the ability of potential customers to safely handle Corfree® M1 prior to commencing a commercial relationship. The Product Stewardship System works with customers to understand their applications and any issues associated with PPE (personal protective equipment), safety equipment (safety showers, eyewash stations, ventilation needs, etc.), storage concerns, disposal requirements, and MSDS questions.

Area and personal air monitoring has been conducted on Corfree® M1 using the NIOSH 0500 - Nuisance Dust - Total Dust and MIE pDR-100AN Personal Particulate Monitor methods. LOGAN (lognormal analysis) is a computerized statistical method for characterizing occupational exposures to chemicals, noise, and other environmental hazards. LOGAN uses sequential collection of data and makes decisions on the minimum amount of data. It helps make cost-effective, accurate decisions that ensure a healthy workplace. LOGAN uses inferential statistics to estimate the true workplace conditions, in the same way that public polling estimates opinions by sampling a representative percentage of the public. LOGAN is designed to limit the risk of employee occupational overexposure to less than 5%.

No specific exposure limits have been established for Corfree® M1. The Permissible Exposure Limit (PEL) for particulates (not otherwise regulated) is 15 mg/m^3, 8-hour TWA, total dust; 5 mg/m^3, 8-hour TWA, respirable dust. The DuPont Acceptable Exposure Limit (AEL) -Total particulate concentration for nuisance dusts should not exceed 10 mg/m^3. None of the samples taken suggest the probability of exposure in excess of the PEL for particulates.

EXPOSURE DATA

Area
C12 Plant Operation 16 Flaker Bay

Operators

People	No. of Results	Avg. of TWA (ppm)	Min. of Results (ppm)	Max. of Results (ppm)
16	6	<0.50 mg/m^3	<0.50 mg/m^3	<0.50 mg/m^3

References for the Summary:

Brock et al. (1984). Biology of Microorganisms, Prentice-Hall, Englewood Cliffs, NJ.

IPCS (n.d.). International Programme on Chemical Safety, SIDS Dossier for Dodecanedioic acid (http://www1.oecd.org/ehs/sidstable/index.htm accessed on November 12, 2002).

Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92.

Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).

TEST PLAN FOR CORFREE® M1

Corfree® M1 CAS No. 72162-23-3	**Data Available**	**Data Acceptable**	**Testing Required**
Study	**Y/N**	**Y/N**	**Y/N**
PHYSICAL/CHEMICAL CHARACTERISTICS			
Melting Point	Y	Y	N
Boiling Point	N/A	N/A	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y*	Y	N
Water Solubility	Y*	Y	N
ENVIRONMENTAL FATE			
Photodegradation	Y	Y	N
Stability in Water	Y	Y	N
Transport (Fugacity)	Y*	Y	N
Biodegradation	Y	Y	N
ECOTOXICITY			
Acute Toxicity to Fish	Y*	Y	N
Acute Toxicity to Invertebrates	Y	Y	N
Acute Toxicity to Aquatic Plants	Y*	Y	N
MAMMALIAN TOXICITY			
Acute Toxicity	Y	Y	N
Repeated Dose Toxicity	Y*	Y	N
Developmental Toxicity	Y*	Y	N
Reproductive Toxicity	Y*	Y	N
Genetic Toxicity Bacterial Gene Mutations	Y	Y	N
Genetic Toxicity Chromosomal Aberrations	Y*	Y	N

Y = Yes
N= No
N/A = Not applicable
Y* = Data available on the largest component of the mixture, DDDA.